REMARKS

Claim 1 has been amended to require that the tumor grows in the live rodent for at least 10 weeks. Support for this amendment is found in the specification in Example 3 in paragraph 55.

As discussed at the interview, this is not a limitation on use, but is a characteristic of the rodent itself — *i.e.*, it must be sufficiently hardy that the tumor continues to grow for at least this length of time.

The Rejection Under 35 U.S.C. § 103

There are only two outstanding bases for rejection, which are substantially the same. The first is for asserted obviousness over the combination of Okabe, *et al., FEBS Lett.* (1997) 467:313-319 in view of WO02/28188 (Kern) and Yang, *et al., PNAS* (2002) 99:3824-3829. This is essentially the same rejection as that made over Okabe and Kern in combination with Verkhusha, *J. Biol. Chem.* (2001) 276:29621-29624.

The Office states that Okabe discloses a rodent that expresses fluorescent protein in all tissues except hair and erythrocytes, although the rodent is not immunocompromised, and that Kern, although entirely prophetic, hypothesizes an immunocompromised mouse that is either heterozygous or homozygous for a selectable marker and that Yang describes the harboring of a tumor in immunocompromised rodents wherein the tumor is itself fluorescent. Verkhusha is simply cited to show that dual imaging is possible, and it somewhat less relevant than Yang.

Applicants believe that the Examiner has correctly characterized the documents made the basis for rejection. Indeed, the elements provided by Okabe and Yang have actually been used in reducing the invention to practice. The issue resides in the lack of predictability of any suggestion

made by Kern that it would be possible to obtain an immunocompromised rodent that is both completely labeled with a fluorescent protein and would be able to remain alive and would support the growth of a labeled tumor for at least 10 weeks.

As discussed at the interview, Kern's suggestion of a nu/nu mouse that is either heterozygous or homozygous for a selectable marker is entirely speculative, and postulates only that the mouse could support a tumor for a time period of one month sufficient to obtain a growth of 1 cm so that the tumor could then be reharvested. See page 11, line 30-page 12, line 1. This is the extent of Kern's speculation. The prophetic example in Kern that involves a fluorescent protein as a selectable marker (example 3) does not even speculate to this extent.

That a stable labeled, immunocompromised rodent could be obtained that would support tumor growth for at least 10 weeks is completely unpredictable. This unpredictability is verified by the demonstration that immunocompromised rodents that are homozygous for the fluorescent protein do not even tolerate tumor implantation and that heterozygosity could surprisingly result in rodents able to support tumor growth for an extended time period. This shows that although immunocompromised rodents are often used to support tumor growth, their ability to do so in the face of an additional handicap — *i.e.*, fluorescently labeled tissues throughout, is not predictable.

Applicants appreciate the willingness of the Examiner to consider the claims with this additional characteristic of the mouse included as a limitation. The suggestion of Kern is only patent defeating if it results in predictable success. Clearly it does not, and this success has been demonstrated by applicants alone.

Reconsideration in light of this amendment is respectfully requested and passage of claims 1-3 and 22-24 to issue is requested as well.

Should minor issues remain that could be resolved by telephone, a telephone call to the undersigned would be greatly appreciated.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 312762004400.

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Respectfully submitted,

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